

## WEST Search History

DATE: Monday, December 18, 2006

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<i>DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI; PLUR=YES; OP=OR</i>			
<input type="checkbox"/>	L4	L3 and desloratadine	49
<input type="checkbox"/>	L3	514/290	837
<input type="checkbox"/>	L2	L1 and desloratadine	7
<input type="checkbox"/>	L1	546/93	283

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NEWS 8 SEP 25 CA(SM)/CAplus(SM) display of CA Lexicon enhanced  
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NEWS 10 SEP 25 CAS REGISTRY(SM) updated with amino acid codes for pyrrolysine  
NEWS 11 SEP 28 CEABA-VTB classification code fields reloaded with new classification scheme  
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NEWS 14 OCT 23 Option to turn off MARPAT highlighting enhancements available  
NEWS 15 OCT 23 CAS Registry Number crossover limit increased to 300,000 in multiple databases  
NEWS 16 OCT 23 The Derwent World Patents Index suite of databases on STN has been enhanced and reloaded  
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NEWS 18 NOV 03 JAPIO enhanced with IPC 8 features and functionality  
NEWS 19 NOV 10 CA/CAplus F-Term thesaurus enhanced  
NEWS 20 NOV 10 STN Express with Discover! free maintenance release Version 8.01c now available  
NEWS 21 NOV 13 CA/CAplus pre-1967 chemical substance index entries enhanced with preparation role  
NEWS 22 NOV 20 CAS Registry Number crossover limit increased to 300,000 in additional databases  
NEWS 23 NOV 20 CA/CAplus to MARPAT accession number crossover limit increased to 50,000  
NEWS 24 DEC 01 CAS REGISTRY updated with new ambiguity codes  
NEWS 25 DEC 11 CAS REGISTRY chemical nomenclature enhanced  
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NEWS 27 DEC 14 GBFULL and FRFULL enhanced with IPC 8 features and functionality

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## L1 STRUCTURE UPLOADED

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=> s 11 ful
FULL SEARCH INITIATED 11:34:00 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      3543 TO ITERATE
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100.0% PROCESSED 3543 ITERATIONS 826 ANSWERS  
SEARCH TIME: 00.00.01

L2 826 SEA SSS FUL L1

10510619

=> file caplus		SINCE FILE	TOTAL
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 FILE LAST UPDATED: 17 Dec 2006 (20061217/ED)

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=> s l2 and pure  
 1287 L2  
 440559 PURE  
 17 PURES  
 440568 PURE  
 (PURE OR PURES)  
 L3 15 L2 AND PURE

=> s l3 and 99.9  
 295294 99  
 1878490 9  
 19884 99.9  
 (99(W)9)  
 L4 0 L3 AND 99.9

=> s l3 and 99  
 295294 99  
 L5 1 L3 AND 99

=> d abs bib hitstr

L5 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2006 ACS on STN  
 AB The present invention provides substantially pure desloratadine having an HPLC purity greater than 99.5% and having an absorbance less than 0.15 Au at 420 nm for a 5 % weight/volume solution in methanol, which does not show a peak for an impurity at a relative retention time in the range from 0.85 to 0.99 (relative to desloratadine appearing at a retention time of 25±5 min), which is greater than the discard limit set at less than 0.025 % of the total area,

when tested according to an HPLC method performed using a Hypersil BDS C8 column (15 cm x 4.6 mm, 5 µm particle size) with the following parameters: Mobile phase: a buffer solution having a pH of about 3, methanol and acetonitrile in a volume ratio of 8:1:1; Injection volume: 20 µL; Flow rate: 1.5 mL/min; Run time: 75 min; Discard limit: Set at less than 0.025% of total area. The present invention also provides a process for the preparation of substantially pure desloratadine by the process comprising acidic hydrolysis of desloratadine analogs with a strong organic acid or a mineral acid.

AN 2003:836755 CAPLUS

DN 139:328323

TI Substantially pure antihistaminic compound

IN Thennati, Rajamannar; Chitturi, Trinadha Rao; Kanangi, Shivramchandra; Unnam, Raja Sekhar; Jadav, Kanaksinh Jesingbhai

PA Sun Pharmaceutical Industries Limited, India

SO PCT Int. Appl., 19 pp.

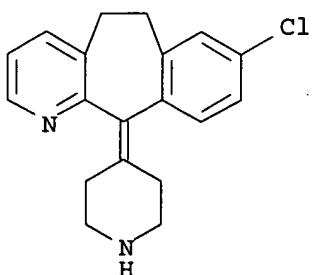
CODEN: PIXXD2

DT Patent

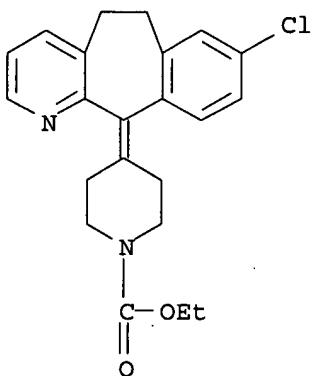
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003086275	A2	20031023	WO 2003-IN156	20030416
	WO 2003086275	A3	20040212		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2003262141	A1	20031027	AU 2003-262141	20030416
	US 2006058334	A1	20060316	US 2004-510619	20041007
PRAI	IN 2002-MU348	A	20020415		
	WO 2003-IN156	W	20030416		
OS	MARPAT 139:328323				
IT	100643-71-8P, Desloratadine				
	RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)				
	(preparation of substantially pure desloratadine by acid hydrolysis)				
RN	100643-71-8 CAPLUS				
CN	5H-Benzo[5,6]cyclohepta[1,2-b]pyridine, 8-chloro-6,11-dihydro-11-(4-piperidinylidene)- (9CI) (CA INDEX NAME)				

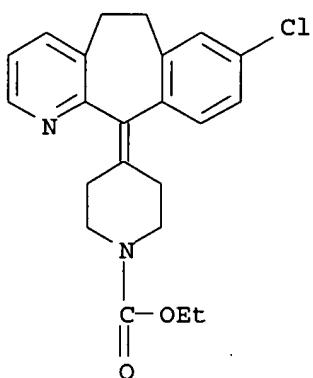


IT 79794-75-5  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (preparation of substantially pure desloratadine by acid hydrolysis)  
 RN 79794-75-5 CAPLUS  
 CN 1-Piperidinecarboxylic acid, 4-(8-chloro-5,6-dihydro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-ylidene)-, ethyl ester (9CI) (CA INDEX NAME)



=> d 13 abs bib fhitstr 1-15

L3 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN  
 AB A review. Since the occurrence of allergic diseases increases, the need for antihistaminic drugs also grows. This requires new and more effective methods for their anal. Electromigration techniques are now often used in pharmaceutical anal. and can complement the use of HPLC. Data from the last 15 yr on the use of electromigration methods (capillary zonal electrophoresis, isotachophoresis, micellar electrokinetic chromatog., capillary electrochromatog.) in the separation and determination of H1-antihistaminics in pure form, drugs, and biol. material are discussed. Data on the anal. of azelastine, cyclizine, diphenhydramine, dioxopromethazine, dimetindene, embramine, pheniramine, hydroxyzine, meclozine, loratadine, and promethazine are examined  
 AN 2006:90923 CAPLUS  
 DN 145:174508  
 TI The use of electromigration methods in analysis of H1-antihistaminics  
 AU Kubacak, P.; Mikus, P.; Valaskova, I.; Havranek, E.  
 CS Farm. Fak., Univ. Komenskeho, Bratislava, Slovakia  
 SO Farmaceuticky Obzor (2005), 74(11), 301-306  
 CODEN: FAOBAS; ISSN: 0014-8172  
 PB Zdravotnickie Vydatelstvo HERBA, spol. s r. o.  
 DT Journal; General Review  
 LA Slovak  
 IT 79794-75-5, Loratadine  
 RL: ANT (Analyte); ANST (Analytical study)  
 (electromigration methods use in anal. of H1-antihistaminic drugs)  
 RN 79794-75-5 CAPLUS  
 CN 1-Piperidinecarboxylic acid, 4-(8-chloro-5,6-dihydro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-ylidene)-, ethyl ester (9CI) (CA INDEX NAME)



L3 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN

AB A rapid, sensitive, accurate, precise, reproducible, and versatile method for determining the purity of reference drug stds. and the routine anal. of illicit

drugs and adulterants using proton (<sup>1</sup>H) NMR Spectroscopy is presented. The methodol. uses a weighed sample dissolved in a deuterated solvent or solvent mixture containing a high purity internal standard. The NMR experiment employs 8

scans using a 45 s delay and 90° pulse. In the determination of purity of reference stds., the number of quant. detns. available is equal to the number of peak

groups that are baseline resolved. The relative standard deviation (RSD) of these signals is usually <1% for pure stds., and the results agree well with other purity determining methods. This method can also aid in the determination of correct mol. weight for stds. containing an unknown number of waters of

hydration or an unknown number of acids per drug in salts. Because the molar response for the hydrogen nucleus is 1 for all compds., and since no separation media are used, only one linearity study is required to test a probe. In the presented study, the linearity of the NMR probe was determined using methamphetamine HCl dissolved in deuterium oxide (D<sub>2</sub>O) with maleic acid as the internal standard (5 mg) for a range of concns. from 0.033 to 69.18 mg/mL with a resulting correlation coefficient of >0.9999 for all 6 methamphetamine peak groups. The spectra of complex illicit heroin, methamphetamine, MDMA, and cocaine samples are presented, as well as an extensive list of compds., their solubilities and the solvent(s) and internal standard used.

AN 2005:1277701 CAPLUS

DN 144:227583

TI Proton nuclear magnetic resonance spectroscopy (NMR) methods for determining the purity of reference drug standards and illicit forensic drug seizures

AU Hays, Patrick A.

CS Drug Enforcement Administration, Special Testing and Research Laboratory, U.S. Department of Justice, Dulles, VA, 20166, USA

SO Journal of Forensic Sciences (2005), 50(6), 1342-1360  
CODEN: JFSCAS; ISSN: 0022-1198

PB ASTM International

DT Journal

LA English

IT 79794-75-5, Loratadine

RL: ANT (Analyte); ANST (Analytical study)

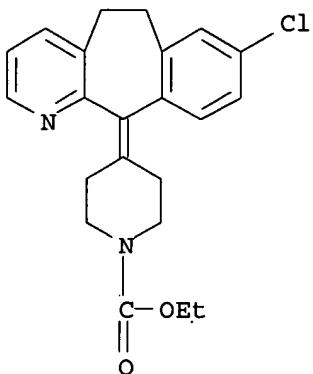
(proton NMR spectroscopy for purity determination of reference drug stds.

and

illicit forensic drug seizures)

RN 79794-75-5 CAPLUS

CN 1-Piperidinecarboxylic acid, 4-(8-chloro-5,6-dihydro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-ylidene)-, ethyl ester (9CI) (CA INDEX NAME)



RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN

AB The inhibitory effects of different antihistamines on the expression of chemokine of cultivated skin in vitro was investigated. The skin was cultivated with mizolastine, cetirizine, loratadine, fexofenadine, dexamethasone and cyclosporin A, resp. Meanwhile histamine and arachidonic acid were added. Twenty-four hours later the total RNAs were obtained and purified with tri-pure isolation reagent. The mRNA expression levels of monocyte chemotactic protein-1 (MCP-1), monocyte chemotactic protein-3 (MCP-3), regulated on activation, normal T cell expressed, and secreted (TANES) and eotaxin were analyzed by RT-PCR methods. The concns. of interleukin (IL)-4, IL-5 and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) in cultivated supernatant were detected by ELISA. In the mizolastine group the MCP-1 mRNA expression was significantly lower than that in cetirizine, loratadine or fexofenadine group and the MCP-3 mRNA expression was significantly lower than that in cetirizine or loratadine group ( $P<0.05$ ). The RANTES mRNA expression and the eotaxin mRNA expression of the mizolastine group was significantly lower than that in loratadine group ( $P<0.05$ ). The level of IL-4 in supernatant in mizolastine group was significantly lower than in fexofenadine group, and the level of IL-5 was significantly lower than that in cetirizine, loratadine and fexofenadine groups, while the level of TNF- $\alpha$  was significantly lower than that in loratadine group. Mizolastine inhibited the expression of chemokines and cytokines more strongly than the other antihistamines.

AN 2005:1140035 CAPLUS

DN 143:415811

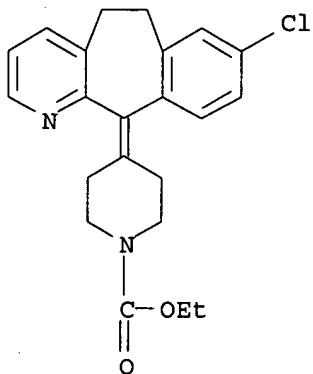
TI Inhibition effects of antihistamines for chemokines and cytokines expression of cultivated skin in vitro

AU Pan, Hu; Hao, Fei

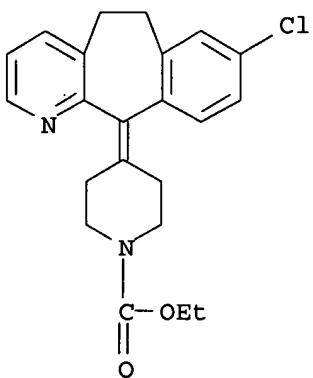
CS Southwest Hospital, Third Military Medical University, Chongqing, 400038, Peop. Rep. China

SO Linchuang Pifuke Zazhi (2005), 34(1), 20-22

CODEN: LPZAEH; ISSN: 1000-4963  
 PB Linchuang Pifuke Zazhi Bianjibu  
 DT Journal  
 LA Chinese  
 IT 79794-75-5, Loratadine  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (inhibition effects of antihistamines for chemokines and cytokines  
 expression of cultivated skin in vitro)  
 RN 79794-75-5 CAPLUS  
 CN 1-Piperidinecarboxylic acid, 4-(8-chloro-5,6-dihydro-11H-  
 benzo[5,6]cyclohepta[1,2-b]pyridin-11-ylidene)-, ethyl ester (9CI) (CA  
 INDEX NAME)



L3 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN  
 AB Two simple extractive spectrophotometric methods were developed for the estimation of loratadine in pure and pharmaceutical dosage forms. These methods are based on the formation of complexes of the drug with the 2 acid dyes Orange-II and Eriochrome Black-T in acidic medium followed by their extraction into chloroform. The absorbance of the chloroform exts. is measured against the corresponding reagent blanks. These methods were statistically evaluated and found to be precise and accurate.  
 AN 2005:261705 CAPLUS  
 DN 142:322948  
 TI Assay of loratadine by extractive spectrophotometry  
 AU Rao, J. V. L. N. Seshagiri; Rao, Y. Srinivasa; Murthy, T. K.; Jitendrababu, V.; Chowdary, K. P. R.  
 CS Department Of Pharmaceutical Sciences, Andhra University, Visakhapatnam, 530 003, India  
 SO Acta Ciencia Indica, Chemistry (2003), 29(3), 207-209  
 CODEN: ACICDV; ISSN: 0253-7338  
 PB Pragati Prakashan  
 DT Journal  
 LA English  
 IT 79794-75-5, Loratadine  
 RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL  
 (Biological study); USES (Uses)  
 (assay of loratadine by extractive spectrophotometry)  
 RN 79794-75-5 CAPLUS  
 CN 1-Piperidinecarboxylic acid, 4-(8-chloro-5,6-dihydro-11H-  
 benzo[5,6]cyclohepta[1,2-b]pyridin-11-ylidene)-, ethyl ester (9CI) (CA  
 INDEX NAME)



RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN

AB A review. Treatment for allergic conjunctivitis has markedly expanded in recent years, providing opportunities for more focused therapy, but often leaving both physicians and patients confused over the variety of options. As monotherapy, oral antihistamines are an excellent choice when attempting to control multiple early-phase, and some late-phase, allergic symptoms in the eyes, nose and pharynx. Unfortunately, despite their efficacy in relief of allergic symptoms, systemic antihistamines may result in unwanted adverse effects, such as drowsiness and dry mouth. Newer second-generation antihistamines (cetirizine, fexofenadine, loratadine and desloratadine) are preferred over older first-generation antihistamines in order to avoid the sedative and anticholinergic effects that are associated with first-generation agents. When the allergic symptom or complaint, such as ocular pruritus, is isolated, focused therapy with topical (ophthalmic) antihistamines. Is often efficacious and clearly superior to systemic antihistamines, either as monotherapy or in conjunction with an oral or intranasal agent. Topical antihistaminic agents not only provide faster and superior relief than systemic antihistamines, but they may also possess a longer duration of action than other classes including vasoconstrictors, pure mast cell stabilizers, NSAIDs and corticosteroids. Many antihistamines have anti-inflammatory properties as well. Some of this anti-inflammatory effect seen with 'pure' antihistamines (levocabastine and emedastine) may be directly attributed to the blocking of the histamine receptor that has been shown to downregulate intercellular adhesion mol.-1 expression and, in turn, limit chemotaxis of inflammatory cells. Some topical multiple-action histamine H1-receptor antagonists (olopatadine, ketotifen, azelastine and epinastine) have been shown to prevent activation of neutrophils, eosinophils and macrophages, or inhibit release of leukotrienes, platelet-activating factors and other inflammatory mediators. Topical vasoconstrictor agents provide rapid relief, especially for redness; however, the relief is often short-lived, and overuse of vasoconstrictors may lead to rebound hyperemia and irritation. Another class of topical agents, mast cell stabilizers (sodium cromoglycate [cromolyn sodium], nedocromil and lodoxamide), may be considered; however, they generally have a much slower onset of action. The efficacy of mast cell stabilizers may be attributed to anti-inflammatory properties in addition to mast cell stabilization. In the class of topical NSAIDs, ketorolac has been promoted for ocular itching but has been found to be

inferior for relief of allergic conjunctivitis when compared with olopatadine and emedastine. Lastly, topical corticosteroids may be considered for severe seasonal ocular allergy symptoms, although long-term use should be avoided because of risks of ocular adverse effects, including glaucoma and cataract formation.

AN 2005:153798 CAPLUS

DN 142:456071

TI Efficacy and tolerability of newer antihistamines in the treatment of allergic conjunctivitis

AU Bielory, Leonard; Lien, Kenneth W.; Bigelsen, Steve

CS Department of Medicine, Pediatrics and Ophthalmology, Division of Allergy, Immunology and Rheumatology, Immuno-Ophthalmology Service, UMDNJ-New Jersey Medical School, Newark, NJ, USA

SO Drugs (2005), 65(2), 215-228

CODEN: DRUGAY; ISSN: 0012-6667

PB Adis International Ltd.

DT Journal; General Review

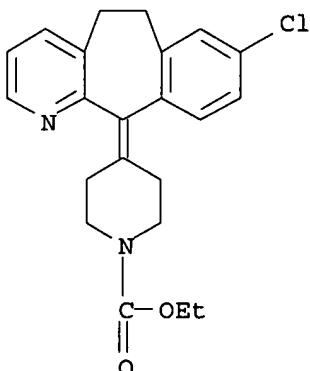
LA English

IT 79794-75-5, Loratadine

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (antihistamines in treatment of allergic conjunctivitis)

RN 79794-75-5 CAPLUS

CN 1-Piperidinecarboxylic acid, 4-(8-chloro-5,6-dihydro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-ylidene)-, ethyl ester (9CI) (CA INDEX NAME)



RE.CNT 110 THERE ARE 110 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN

AB The invention relates to novel microemulsions comprising a non-polar lipid, at least one polar solvent, a surfactant, and a polar lipid. A microemulsion of these ingredients provides an environment that substantially encloses airborne particles, i.e., allergens, bacteria and viruses, and it can be used for entrapping such particles. The inventive microemulsions are especially adapted for the prevention of symptoms in mammals, which are indirectly or directly caused by airborne particles. The invention further provides compns. comprising such microemulsions and methods of treatment comprising administering the same. For example, a microemulsion was prepared, containing glycerol monooleate 34%, propylene glycol

23%, polyethylene glycol 400 18%, sesame oil 11%, saline solution 10%, and polysorbate 80 4%. The microemulsion was administered as a spray to human volunteers. No signs or complaints of adverse effects were made. The formulation showed a superior wetting as compared with sesame oil and pure saline. Similar formulations protected MDCK and HSG cells in the culture from infection with influenza A virus.

AN 2005:55045 CAPLUS  
 DN 142:141249  
 TI Microemulsions comprising lipids for preventing airway diseases  
 IN Cockbain, Julian; Wollmer, Per; Andersson, Morgan; Greiff, Lennart; Landh, Thomas

PA Nares AB, Swed.

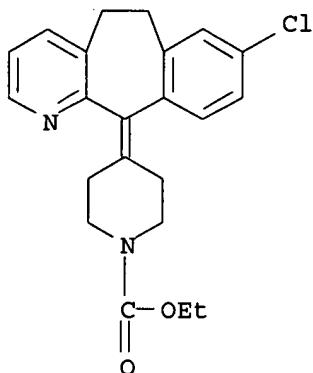
SO PCT Int. Appl., 36 pp.  
 CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005004843	A1	20050120	WO 2004-GB2925	20040707
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1648412	A1	20060426	EP 2004-743268	20040707
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
	US 2006269578	A1	20061130	US 2006-563828	20060508
PRAI	SE 2003-2005	A	20030707		
	SE 2003-2006	A	20030707		
	US 2003-484664P	P	20030707		
	WO 2004-GB2925	W	20040707		
IT	79794-75-5, Loratadine				
	RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (microemulsions comprising lipids, polar solvent, and surfactant for entrapping airborne particles and preventing airway diseases)				
RN	79794-75-5 CAPLUS				
CN	1-Piperidinecarboxylic acid, 4-(8-chloro-5,6-dihydro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-ylidene)-, ethyl ester (9CI) (CA INDEX NAME)				



RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN  
AB A consumable film adapted to adhere to and dissolve in the oral cavity of a warm-blooded animal including humans, comprising a modified starch, pharmaceutically active agent and, optionally, at least one water-soluble polymer, such as pullulan, cellulose derivs., polyvinylpyrrolidone, acacia gum, poly(acrylic acid), etc. For example, preparation of a quick dissolving consumable film containing 15.0 mg dextromethorphan-HBr and Pure -Cote B793 base, using xanthan gum, locust bean gum, carrageenan and Pure-Cote B793 as film-forming ingredients was presented.

AN 2004:965039 CAPLUS

DN 141:400962

TI Fast dissolving orally consumable films containing a modified starch for improved heat and moisture resistance

IN Fadden, David John; Kulkarni, Neema Mahesh; Sorg, Albert Frank

PA Warner-Lambert Company LLC, USA

SO PCT Int. Appl., 33 pp.

CODEN: PIXXD2

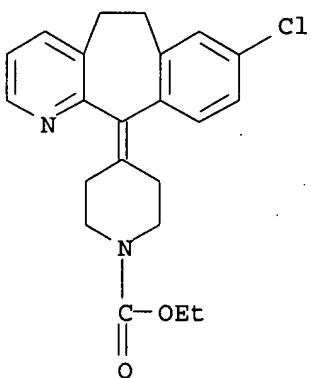
DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004096193	A1	20041111	WO 2004-IB1398	20040419
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU	2004233744	A1	20041111	AU 2004-233744	20040419
CA	2523372	A1	20041111	CA 2004-2523372	20040419
EP	1622595	A1	20060208	EP 2004-728218	20040419
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
BR	2004009463	A	20060502	BR 2004-9463	20040419
CN	1784218	A	20060607	CN 2004-80011888	20040419

JP 2006525308	T	20061109	JP 2006-506579	20040419
US 2004247648	A1	20041209	US 2004-838045	20040503
PRAI US 2003-467339P	P	20030502		
WO 2004-IB1398	A	20040419		
IT 79794-75-5, Loratadine				
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (fast dissolving oral films containing modified starch and optionally water-soluble polymer for improved heat and moisture resistance)				
RN 79794-75-5 CAPLUS				
CN 1-Piperidinecarboxylic acid, 4-(8-chloro-5,6-dihydro-11H- benzo[5,6]cyclohepta[1,2-b]pyridin-11-ylidene)-, ethyl ester (9CI) (CA INDEX NAME)				



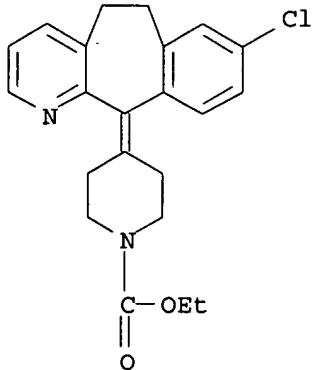
RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN  
 AB Disclosed is a free-flowing solid formulations of drugs or pharmaceutical agents which have poor aqueous solubility are obtained by admixing a liquid or gel composition that includes 1-30 % of the drug, 5-60 % of a surfactant, 10-40 % of water; 1-20 % of unsatd. fatty acid ester, 0-50 % water miscible pharmaceutically acceptable polyol and 1-10 % phospholipid with a pharmaceutically acceptable suitable solid carrier and thereafter drying the admixt. The free-flowing powder is suitable for being formed into tablets or capsules. The drug or pharmaceutical agent is solubilized in the formulation and has significantly improved bio-availability when compared to the drug tested in its pure form. A gel composition containing polyoxyethylene sorbitan monooleate 35, propylene glycol 25, Et linoleate 8, simvastatin 4, and 5 % lecithin aqueous solution q.s. to 100 % was formulated. Colloidal silicon dioxide 30 parts was granulated with the obtained gel 70 parts. The granules was dried to provide a free-flowing powder. When this powder was exposed to a gastric medium of pH 1.2, 67 % of the drug simvastatin dissolved within 10 min.  
 AN 2004:490267 CAPLUS  
 DN 141:42919  
 TI Free-flowing solid formulations with improved bio-availability of poorly water soluble drugs and process for making the same  
 IN Li, Wenji; Alosio, Edward; Dema-Ala, Bricini Faith; Nguyen, Amy  
 PA USA  
 SO U.S. Pat. Appl. Publ., 9 pp.  
 CODEN: USXXCO  
 DT Patent

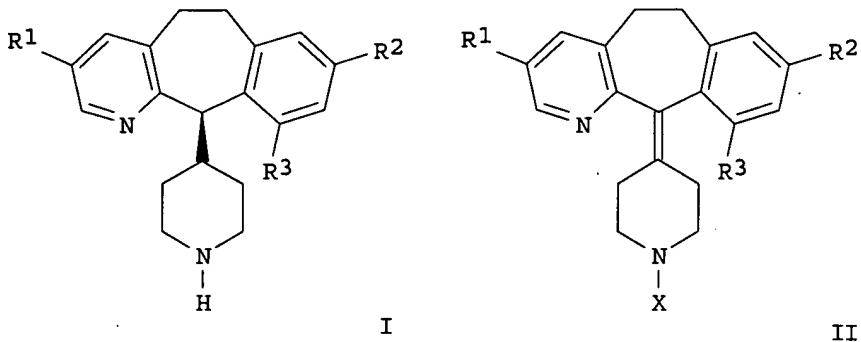
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	US 2004115226	A1	20040617	US 2002-317657	20021212	
	WO 2004054540	A2	20040701	WO 2003-US38979	20031209	
	WO 2004054540	A3	20040930			
		W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW			
		RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
		AU 2003300833	A1	20040709	AU 2003-300833	20031209
		JP 2006511536	T	20060406	JP 2004-560372	20031209
		US 2006263397	A1	20061123	US 2006-494131	20060727
	PRAI	US 2002-317657	A	20021212		
		WO 2003-US38979	W	20031209		
IT	79794-75-5, Loratadine					
	RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (free-flowing solid formulations with improved bio-availability of poorly water soluble drugs obtained from gel compns. containing surfactants, fatty acid esters, polyols, and phospholipids)					
RN	79794-75-5 CAPLUS					
CN	1-Piperidinecarboxylic acid, 4-(8-chloro-5,6-dihydro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-ylidene)-, ethyl ester (9CI) (CA INDEX NAME)					



L3 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN  
GI



**AB** Title compds. I [R1, R2, R3 = halo, alkyl, OR4; R4 = alkyl; X = H] were prepared via the reduction (+) piperidinyldenes II. For example, diisobutylaluminum hydride reduction of atropisomer (+) II (R1, R3 = Br; R2 = Cl; X = H), e.g., prepared from piperidinecarboxylic acid II (R1, R3 = Br; R2 = Cl; X = CO<sub>2</sub>Et) in 2-steps, afforded claimed piperidine I (R1, R3 = Br; R2 = Cl; X = H) in  $[\alpha]$  = +51.9°. Of note, atropisomer (-) II (R1, R3 = Br; R2 = Cl; X = H) was converted in 45% yield to (+) II (R1, R3 = Br; R2 = Cl; X = H) via heating in 1,2-dichlorobenzene at 150° C for 7-days. Compds. I are useful intermediates in the preparation of farnesyl protein transferase (FPT) inhibitor SCH66336.

**AN** 2004:212161 CAPLUS

**DN** 140:270738

**TI** Preparation of optically pure atropisomers of the piperidinylidenebenzocycloheptapyridine intermediate of SCH66336

**IN** Njoroge, F. George; Vibulbhan, Bancha; Girijavallabhan, Viyyoor M.

**PA** Schering Corporation, USA

**SO** U.S., 7 pp.

CODEN: USXXAM

**DT** Patent

**LA** English

**FAN.CNT** 1

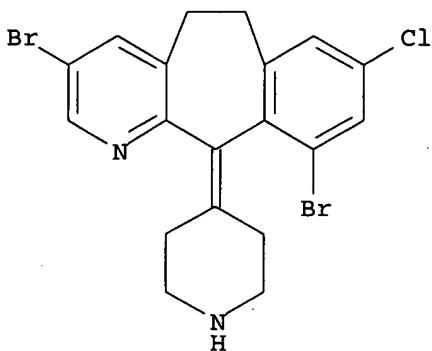
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6706883	B1	20040316	US 1999-345966	19990701
PRAI	US 1998-91585P	P	19980702		
OS	CASREACT 140:270738; MARPAT 140:270738				
IT	218453-59-9P				

RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)

(preparation of optically pure atropisomers of the piperidinylidenebenzocycloheptapyridine intermediate of SCH66336)

**RN** 218453-59-9 CAPLUS

**CN** 5H-Benzocyclohepta[1,2-b]pyridine, 3,10-dibromo-8-chloro-6,11-dihydro-11-(4-piperidinylidene)-, (+)- (9CI) (CA INDEX NAME)



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN

AB The present invention provides substantially pure desloratadine having an HPLC purity greater than 99.5% and having an absorbance less than 0.15 Au at 420 nm for a 5 % weight/volume solution in methanol, which does not show a peak for an impurity at a relative retention time in the range from 0.85 to 0.99 (relative to desloratadine appearing at a retention time of 25±5 min), which is greater than the discard limit set at less than 0.025 % of the total area, when tested according to an HPLC method performed using a Hypersil BDS C8 column (15 cm x 4.6 mm, 5 µm particle size) with the following parameters: Mobile phase: a buffer solution having a pH of about 3, methanol and acetonitrile in a volume ratio of 8:1:1; Injection volume: 20 µL; Flow rate: 1.5 mL/min; Run time: 75 min; Discard limit: Set at less than 0.025% of total area. The present invention also provides a process for the preparation of substantially pure desloratadine by the process comprising acidic hydrolysis of desloratadine analogs with a strong organic acid or a mineral acid.

AN 2003:836755 CAPLUS

DN 139:328323

TI Substantially pure antihistaminic compound

IN Thennati, Rajamannar; Chitturi, Trinadha Rao; Kanangi, Shivramchandra; Unnam, Raja Sekhar; Jadav, Kanaksinh Jesingbhai

PA Sun Pharmaceutical Industries Limited, India

SO PCT Int. Appl., 19 pp.

CODEN: PIXXD2

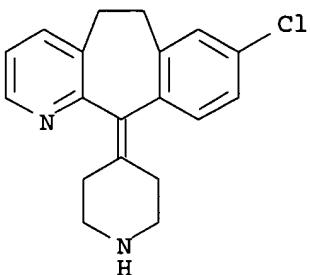
DT Patent

LA English

FAN.CNT 1

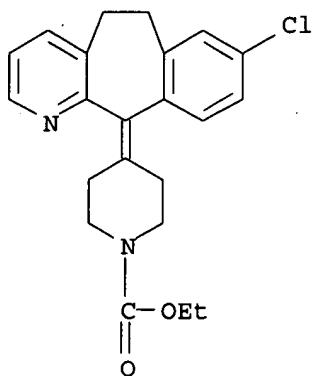
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003086275	A2	20031023	WO 2003-IN156	20030416
	WO 2003086275	A3	20040212		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	AU 2003262141	A1	20031027	AU 2003-262141	20030416

US 2006058334 A1 20060316 US 2004-510619 20041007  
 PRAI IN 2002-MU348 A 20020415  
 WO 2003-IN156 W 20030416  
 OS MARPAT 139:328323  
 IT 100643-71-8P, Desloratadine  
 RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use);  
 BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of substantially pure desloratadine by acid  
 hydrolysis)  
 RN 100643-71-8 CAPLUS  
 CN 5H-Benzocyclohepta[1,2-b]pyridine, 8-chloro-6,11-dihydro-11-(4-  
 piperidinylidene)- (9CI) (CA INDEX NAME)



L3 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN  
 AB Three simple and accurate methods are presented for determination of  
 Cetirizine,  
 Fexofenadine, Loratadine and Acrivastine in pure form and com.  
 dosage forms. The first method is based on the reaction of the above  
 cited drugs with bromocresol purple dye to form ion-pair complex  
 extractable with chloroform and subsequently measured  
 spectrophotometrically. Secondly, eosin gives with these drugs ion-pair  
 complex, measurable directly without extraction both spectrophotometrically and  
 spectrofluorimetrically. The last method involves the base-catalyzed  
 condensation of mixed anhydrides of organic acids (citric acid/acetic  
 anhydride) where as the tertiary amino group in the above-cited drugs acts  
 as the basic catalyst. The product of condensation is measured  
 spectrophotometrically. All the reaction conditions for the proposed  
 method were studied.  
 AN 2002:742231 CAPLUS  
 DN 138:193370  
 TI Determination of some histamine H1-receptor antagonists in dosage forms  
 AU Gazy, Azza A.; Mahgoub, Hoda; El-Yazbi, F. A.; El-Sayed, M. A.; Youssef,  
 Rasha M.  
 CS Faculty of Pharmacy, Department of Pharmaceutical Analytical Chemistry,  
 University of Alexandria, Alexandria, 21521, Egypt  
 SO Journal of Pharmaceutical and Biomedical Analysis (2002), 30(3), 859-867  
 CODEN: JPBADA; ISSN: 0731-7085  
 PB Elsevier Science B.V.  
 DT Journal  
 LA English  
 IT 79794-75-5, Loratadine  
 RL: ANT (Analyte); ANST (Analytical study)  
 (determination of some H1 antihistamines by fluorometry and spectroscopy)  
 RN 79794-75-5 CAPLUS  
 CN 1-Piperidinecarboxylic acid, 4-(8-chloro-5,6-dihydro-11H-

benzo[5,6]cyclohepta[1,2-b]pyridin-11-ylidene)-, ethyl ester (9CI) (CA INDEX NAME)



RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN

AB Four stability-indicating procedures have been suggested for determination of the non sedating antihistaminic agent loratadine. Loratadine being an ester undergoes alkaline hydrolysis and the corresponding acid derivative is produced as

a degradation product. Its identity was confirmed using IR and MS. The first procedure is based on determination of loratadine by HPLC with detection at wavelength, 250 nm. Mobile phase is acetonitrile:orthophosphoric acid (35:65) using benzophenone as an internal standard. Sensitivity range is 5.00-50.00 µg/mL. Second determination is a densitometric procedure based on determination of loratadine in the presence of its degradate at λ 246 nm using the mobile phase; methanol:ammonia (10:0.15). Sensitivity range is 1.25-7.50 µg per spot. The third procedure is a spectrophotometric one where a mixture of loratadine and its degradate are resolved by first derivative

ratio spectra. Sensitivity range is found to be 3.00-22.00 µg/mL, upon carrying out the measurements at wavelengths 236, 262.4 and 293.2 nm. The fourth procedure is based on second derivative spectrophotometry, where D2 measurements are carried out at λ 266 nm. The sensitivity range is 3.00-22.00 µg/mL. The validity of the described procedures was assessed by applying the standard addition technique. Statistical anal. of the results have been carried out revealing high accuracy and good precision. The suggested procedures could be used for determination of loratadine both in pure and dosage forms, as well as in the presence of its degradate.

AN 2002:418184 CAPLUS

DN 137:253110

TI Stability indicating methods for the determination of loratadine in the presence of its degradation product

AU El Ragehy, N. A.; Badawy, A. M.; Khateeb, S. Z.-El

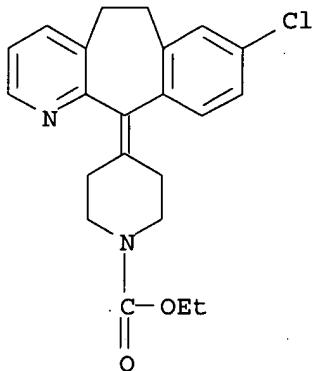
CS Faculty of Pharmacy, Department of Analytical Chemistry, Cairo University, Cairo, 11562, Egypt

SO Journal of Pharmaceutical and Biomedical Analysis (2002), 28(6), 1041-1053  
CODEN: JPBADA; ISSN: 0731-7085

PB Elsevier Science B.V.

DT Journal

LA English  
 IT 79794-75-5, Loratadine  
 RL: ANT (Analyte); ANST (Analytical study)  
 (determination of loratadine in presence of degradation product by HPLC and  
 second derivative spectrophotometry)  
 RN 79794-75-5 CAPLUS  
 CN 1-Piperidinecarboxylic acid, 4-(8-chloro-5,6-dihydro-11H-  
 benzo[5,6]cyclohepta[1,2-b]pyridin-11-ylidene)-, ethyl ester (9CI) (CA  
 INDEX NAME)

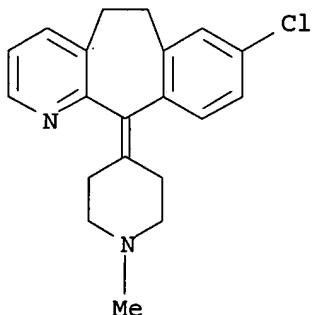


RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 13 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN  
 AB To be considered for further development, lead structures should display the following properties: (1) simple chemical features, amenable for chemical optimization; (2) membership to an established SAR series; (3) favorable patent situation; and (4) good absorption, distribution, metabolism, and excretion (ADME) properties. There are two distinct categories of leads: those that lack any therapeutic use (i.e., "pure" leads), and those that are marketed drugs themselves but have been altered to yield novel drugs. We have previously analyzed the design of leadlike combinatorial libraries starting from 18 lead and drug pairs of structures (S. J. Teague et al. Angew. Chemical, Int. Ed. Engl. 1999, 38, 3743-3748). Here, we report results based on an extended dataset of 96 lead-drug pairs, of which 62 are lead structures that are not marketed as drugs, and 75 are drugs that are not presumably used as leads. We examined the following properties: MW (mol. weight), CMR (the calculated mol. refractivity), RNG (the number of rings), RTB (the number of rotatable bonds), the number of hydrogen bond donors (HDO) and acceptors (HAC), the calculated logarithm of the n-octanol/water partition (CLogP), the calculated logarithm of the distribution coefficient at pH 7.4 (LogD74), the Daylight-fingerprint druglike score (DFPS), and the property and pharmacophore features score (PPFS). The following differences were observed between the medians of drugs and leads:  $\Delta\text{MW} = 69$ ;  $\Delta\text{CMR} = 1.8$ ;  $\Delta\text{RNG} = \Delta\text{HAC} = 1$ ;  $\Delta\text{RTB} = 2$ ;  $\Delta\text{CLogP} = 0.43$ ;  $\Delta\text{LogD74} = 0.97$ ;  $\Delta\text{HDO} = 0$ ;  $\Delta\text{DFPS} = 0.15$ ;  $\Delta\text{PPFS} = 0.12$ . Lead structures exhibit, on the average, less mol. complexity (less MW, less number of rings and rotatable bonds), are less hydrophobic (lower CLogP and LogD74), and less druglike (lower druglike scores). These findings indicate that the process of optimizing a lead into a drug results in more complex structures. This information should be used in the design of novel combinatorial libraries

that are aimed at lead discovery.

AN 2001:527755 CAPLUS  
 DN 135:266637  
 TI Is There a Difference between Leads and Drugs? A Historical Perspective  
 AU Oprea, Tudor I.; Davis, Andrew M.; Teague, Simon J.; Leeson, Paul D.  
 CS AstraZeneca R&D Molndal EST Lead Informatics, Moelndal, S 431 83, Swed.  
 SO Journal of Chemical Information and Computer Sciences (2001), 41(5),  
 1308-1315  
 CODEN: JCISD8; ISSN: 0095-2338  
 PB American Chemical Society  
 DT Journal  
 LA English  
 IT 38092-89-6  
 RL: PRP (Properties)  
 (drug design and structure-activity relationship between leads and  
 leadlike drugs)  
 RN 38092-89-6 CAPLUS  
 CN 5H-Benzocyclohepta[1,2-b]pyridine, 8-chloro-6,11-dihydro-11-(1-methyl-  
 4-piperidinylidene)- (9CI) (CA INDEX NAME)

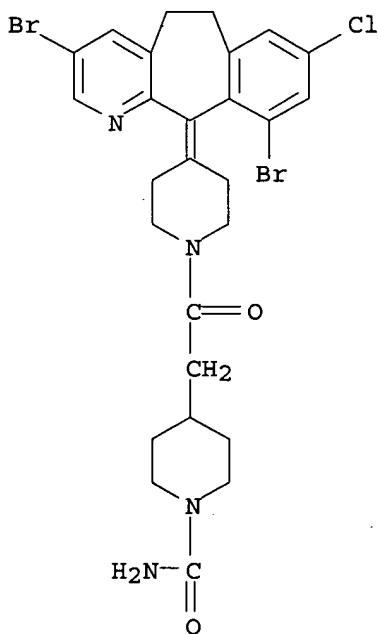


RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN  
 AB Introduction of bromine at the 10-position of 3-bromo-8-  
 chlorobenzocycloheptapyridine analogs results in formation of racemic  
 atropisomeric compds. that are easily separable at room temperature on a  
 ChiralPak AD column providing pure atropisomers. Evaluation of  
 the FPT (farnesyl protein transferase) activity of these atropisomers  
 revealed that dextrorotatory compds. were more potent in the farnesyl  
 protein transferase enzyme and cellular assay than their levorotatory  
 isomers. The dextrorotatory were found to inhibit farnesyl protein  
 transferase processing in COS cells at low micro molar range. They were  
 also found to have excellent cellular antitumor activity. Evaluation of  
 the dextrorotatory isomers in DLD-tumor model in nude mice revealed that  
 they were efficacious, inhibiting tumor growth by 55 and 63% at 50 mpk,  
 resp.  
 AN 1999:383510 CAPLUS  
 DN 131:157697  
 TI Atropisomeric trihalobenzocycloheptapyridine analogues provide  
 stereoselective FPT inhibitors with antitumor activity  
 AU Njoroge, F. George; Vibulbhan, Bancha; Bishop, W. Robert; Kirschmeier,  
 Paul; Bryant, Mathew S.; Nomeir, Amin A.; Liu, Ming; Doll, Ronald J.;  
 Girijavallabhan, Viyyoor M.; Ganguly, Ashit K.  
 CS Departments of Chemistry and Tumor Biology, Schering-Plough Research

SO Institute, NJ, 07033, USA  
 SO Bioorganic & Medicinal Chemistry (1999), 7(5), 861-867  
 CODEN: BMECEP; ISSN: 0968-0896  
 PB Elsevier Science Ltd.  
 DT Journal  
 LA English  
 IT 193275-78-4P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation and farnesyl protein transferase inhibiting activity of atropisomeric trihalobenzocycloheptapyridine analogs)

RN 193275-78-4 CAPLUS  
 CN 1-Piperidinecarboxamide, 4-[2-[4-(3,10-dibromo-8-chloro-5,6-dihydro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-ylidene)-1-piperidinyl]-2-oxoethyl]-(9CI) (CA INDEX NAME)

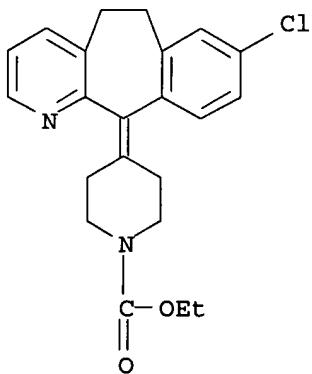


RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN  
 AB The antihistamine-H1 and antiplatelet activating factor (PAF) activities of seven compds., including rupatadine, a new antiallergic drug, were studied in healthy beagle dogs using a new exptl. model that allows simultaneous testing of PAF and histamine reactions in the same animal. The method was based on the measurement of wheal area induced in dogs' skin by intradermal injection of PAF (1.5 µg) or histamine (2.5 µg). Rupatadine and the H1-antihistamine drugs cetirizine, levocabastine, and loratadine, administered orally at doses of 1 or 10 mg/kg showed similar maximum potencies (75-85% of wheal inhibition) 4-8 h after treatment. Levocabastine was the longest-acting compound (55% and 69% inhibition 24 h after administration of 1 or 10 mg/kg, resp.). Rupatadine, loratadine, and cetirizine behaved similarly, showing 34% and 58% inhibition at 24 h

at the same doses. Dual PAF and histamine antagonist SCH-37370 exhibited mild anti-H1 activity, the maximum effect being 27% at 10 mg/kg. Pure PAF antagonists WEB-2086 and SR-27417 showed no effect against histamine-induced wheals. Only rupatadine, SR-27417A, SCH-37370, and WEB-2086 showed PAF antagonist activity, whereas pure antihistamines were inactive. The most potent PAF antagonist was SR-27417A, with a maximum effect of 56% and 80% at 1 and 10 mg/kg, resp. Rupatadine and WEB-2086 antagonized PAF-induced wheal response, although they showed less maximum effect and shorter duration of action than SR-27417A. SCH-37370 exhibited only slight PAF antagonist activity at 10 mg/kg. Overall, the histamine- and PAF-induced wheal model in dogs proved useful for independent evaluation of histamine and PAF antagonist properties of the tested compds., as pure antagonists blocked the effect of only one of the mediators. Rupatadine was the only of the seven compds. studied that showed potent dual activity against PAF and histamine.

AN 1997:112567 CAPLUS  
 DN 126:207287  
 TI Dual effect of a new compound, rupatadine, on edema induced by platelet-activating factor and histamine in dogs: comparison with antihistamines and PAF antagonists  
 AU Queralt, Mireia; Merlos, Manuel; Giral, Marta; Puigdemont, Anna  
 CS Departamento de Farmacología, Facultad de Veterinaria, Universidad Autónoma de Barcelona, Barcelona, Spain  
 SO Drug Development Research (1996), 39(1), 12-18  
 CODEN: DDREDK; ISSN: 0272-4391  
 PB Wiley-Liss  
 DT Journal  
 LA English  
 IT 79794-75-5, Loratadine  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
 (dual effect of a new compound, rupatadine, on edema induced by platelet-activating factor and histamine in dogs and comparison with antihistamines and PAF antagonists)  
 RN 79794-75-5 CAPLUS  
 CN 1-Piperidinecarboxylic acid, 4-(8-chloro-5,6-dihydro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-ylidene)-, ethyl ester (9CI) (CA INDEX NAME)



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